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The rise of blockbuster pharmaceutical acquisitions has prompted fears that unprecedented market concentration will weaken competition. Two of the most prominent concerns focus on the upstream and downstream ends of the pharmaceutical industry: (1) the concern that these mergers will concentrate the market for discovery and will therefore lead to fewer discoveries; and (2) the concern that merging large marketing, sales, and distribution forces will strengthen the hands of select pharmaceutical manufacturers and weaken downstream competition. Having considered potential dynamic effects in the industry and conducted a series of preliminary interviews with knowledgeable observers, though, this Article argues that neither of these common fears is systematically warranted. There are, however, potential dangers in market concentration at an intermediate stage during the discovery-to-development path: the stage for regulatory approval. These preliminary findings are a product of dramatic changes that are currently reshaping the structure of the pharmaceutical industry. This Article discusses how these structural changes contribute to the current merger wave, how dynamic responses by industry players in response to the merger wave mitigate the potential harm from competition, and how the political arena might still offer threats to market concentration.

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INTRODUCTION

The pharmaceutical industry's contributions to global health and economic development make it one of the most important commercial sectors in the world. Worldwide sales of pharmaceutical products reached about \$1 trillion in 2015,¹ and the value of the industry's many lifesaving discoveries vastly exceeds that figure.

At the same time, the sector is also highly controversial and has long raised concerns about pricing, marketing, and product development strategies. The industry recently triggered renewed criticism when firms such as Turing, Horizon, and Valeant engineered dramatic price increases for generic products, and Gilead and Mylan made significant price demands for specialized drugs for Hepatitis C treatments and the EpiPen.² With a renewed sense that reducing pharmaceutical prices is central to making health care affordable, and with a renewed hope that vigorous antitrust enforcement might lead the way, these events reminded policymakers and antitrust practitioners of the importance of mergers and acquisitions ("M&A") by pharmaceutical firms.

Although M&A have been a staple in the pharmaceutical industry for over a century, recent mergers of industry giants—particularly over the past decade or so—mark an unprecedented level of consolidation. Giants are now acquiring other giants, and concern has appropriately emerged for whether such acquisitions harm the competitive marketplace and

1. QUINTILESIMS, TOP LINE MARKET DATA: TOP 20 GLOBAL PRODUCTS 2015, 1, https://www.imshealth.com/files/web/Corporate/News/Top-Line%20Market%20Data/Top_20_Global_Products_2015.pdf (last visited May 16, 2017).

2. Daniel Kozarich, *Mylan's EpiPen Pricing Crossed Ethical Boundaries*, FORTUNE (Sept. 27, 2016), <http://fortune.com/2016/09/27/mylan-epipen-heather-bresch/>; Robert Langreth, *How Gilead Priced Its \$20 Billion Blockbuster*, BLOOMBERG (Dec. 10, 2015, 4:37 PM), <http://www.bloomberg.com/news/articles/2015-12-10/behind-the-1-000-pill-a-formula-for-profits-inside-gilead>; Johnathan D. Rockoff & Ed Silverman, *Pharmaceutical Companies Buy Rivals' Drugs, Then Jack Up the Prices*, WALL ST. J. (Apr. 26, 2015, 9:00 PM), <http://www.wsj.com/articles/pharmaceutical-companies-buy-rivals-drugs-then-jack-up-the-prices-1430096431>; *Valeant & Shkreli-led Turing Bought Drugs to Hike Prices, Documents Allege*, CBC NEWS (Feb. 2, 2016, 2:39 PM), <http://www.cbc.ca/news/business/drug-prices-shkreli-valeant-turing-1.3430639> [hereinafter *Valeant & Shkreli-led Turing*].

innovation pipelines.

Fears that mergers will weaken competition raise two predominant concerns, each respectively focusing on the upstream and downstream ends of the pharmaceutical industry. Upstream, the fear is that mergers of large research and development (“R&D”) operations might concentrate the market for discovery, reduce competition and experimentation for new discoveries, and therefore lead to fewer discoveries. Downstream, the concern is that merging large marketing, sales, and distribution forces might strengthen the hands of select pharmaceutical manufacturers and weaken downstream competition, which could then reduce pricing pressures and increase distribution barriers to innovative new competitors. These concerns prompted some policymakers and consumer activists to warn that merger activity in the pharmaceutical sector is reaching a tipping point that threatens increased prices, reduces incentives for innovation, and reveals other structural reckonings in the industry.³

By contrast, other voices are less concerned about the mergers. Rather than reduce innovativeness, mergers might generate more productive focus and greater economies of scale that actually promote development activities. And rather than reduce competition and experimentation, mergers might open doors for innovative new entrants. Thus, both policy and corporate strategy would benefit from a deeper understanding of when mergers will harm competition and when they might benefit the larger marketplace.

This Article reviews theory and some evidence that articulates the likely consequences of M&A deals in the pharmaceutical industry. It offers an exploratory analysis of industry trends and concludes that M&A activity appears to play only a limited role in current pricing controversies, although antitrust caution is relevant with some targeted deals. The stakes for innovative activity, meanwhile, are higher, but this Article’s analysis suggests that merger activity is frequently associated with more active product pipelines and appears central to an ongoing innovation strategy in a dynamic global scientific and market environment. In some conditions, though, M&A activity may create risks of dampening innovative capability, so that there is some potential for antitrust assessment of R&D productivity. The implications from our findings suggest an industry where most acquisitions are a product of important technological and geopolitical changes, rather than a tool to

3. Peter Young, *Biotech Financial and M&A Trends—Two Steps Forward, One Step Back*, PHARMEXEC.COM (Apr. 1, 2016), <http://www.pharmexec.com/biotech-financial-and-ma-trends-two-steps-forward-one-step-back>.

consolidate pricing or market power. We do, however, find some potential dangers in market concentration at an intermediate stage during the discovery-to-development path: the stage for regulatory approval.

This Article begins with an overview of the industry's recent surge in M&A activity. It then examines whether this M&A activity increased industry-wide concentration, increased prices, or reduced innovative output. After exploring suggestive empirical evidence that industry M&A activity has led to neither industry-wide price increases nor a reduction in innovation, this Article explores two alternative and less traditional anticompetitive concerns from industry megamergers: industry concentration in marketing, sales and distribution of pharmaceuticals, and concentration in the regulatory process of seeking approval for new products. Overall, the sector's history and performance suggest nuanced implications for antitrust policy in the pharmaceutical sector, as policy ought to pay careful attention to certain regulatory and market structures as well as broad trends in a changing global industry.

I. BACKGROUND: TRENDS IN PHARMACEUTICAL MERGERS & ACQUISITIONS

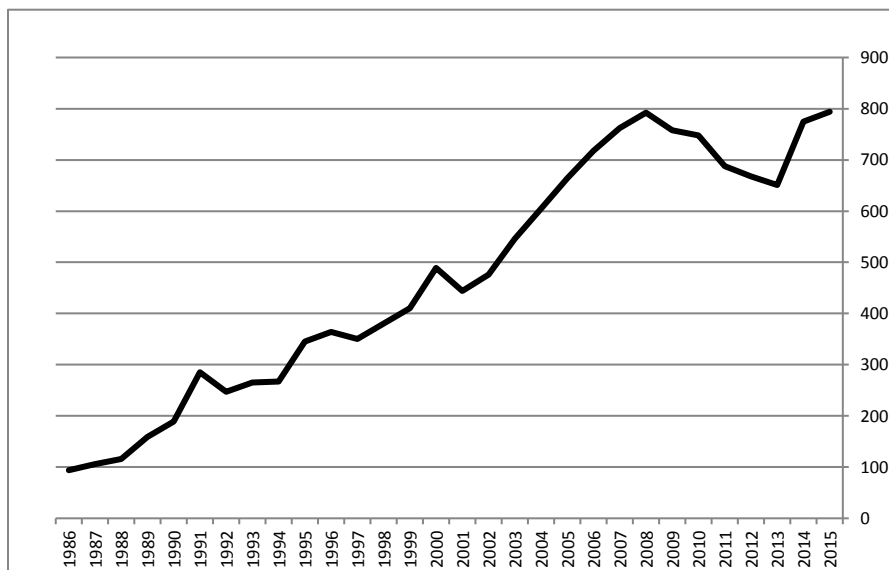
M&A deals in the pharmaceutical industry date back to the industry's origins. The four companies of Glaxo, Wellcome, Beecham, and SmithKline typify the industry's development. Each of the four companies began in the early 1800s, and grew by making between six and eleven significant acquisitions, as well as many dozens of smaller acquisitions, through the 1980s. But as the industry approached the later part of the twentieth century, the trend of commonplace acquisitions was supplemented with what are commonly called "blockbuster mergers." In 1989, SmithKline merged with Beecham in a \$7.7 billion deal; in 1995, Glaxo merged with Wellcome in a \$15 billion deal; and in 2000, Glaxo-Wellcome merged with SmithKline-Beecham in a (then-unprecedented) \$76 billion deal.⁴

This history not only reveals that pharmaceutical acquisitions are as old as the industry, but it also reflects how M&A activity has steadily increased since the 1980s. The blockbuster merger trend continued through 2008, which exhibited fifteen megadeals that each totaled over \$1 billion, led by the Roche's acquisition of Genentech for nearly \$100 billion, and reached historic highs in both numbers and values of deals in

4. The mergers and acquisitions ("M&A") deal that created GlaxoSmithKline ("GSK") in 2000 was the latest in more than fifty substantial deals since 1859 involving predecessors of the company, including Glaxo, Wellcome, Beckman, Beecham, and SmithKline.

recent years.⁵ Figure 1 illustrates the growth in pharmaceutical M&A activity and reveals that the number of annual deals grew from approximately one hundred deals in the late 1980s, to almost 800 deals in 2015.⁶ Industry-wide deal value reached almost \$400 billion in 2015, for about 250 deals with reported value.⁷

FIGURE 1: Global Trends in Announced Pharma M&A (Acquirer in Standard Industry Classification (“SIC”) 2834), 1986–2015.⁸



A conventional wisdom developed to describe the recent emergence of megamergers. To extract maximum value from blockbuster drugs, firms invest sunk costs in marketing and distribution. When a firm’s blockbuster drug loses its patent protection, the firm needs to find other high-volume, high-margin drugs to supply its marketing mechanisms. If it has no compounds within its development pipeline that can suitably utilize these mechanisms, the firm purchases another pharmaceutical company that owns patents for major compounds that can utilize its

5. James Fontanella-Khan, *Pharma M&A for 2016 Continues to Surge*, FIN. TIMES (Feb. 1, 2016), <https://www.ft.com/content/9adbce94-c902-11e5-be0b-b7ece4e953a0>.

6. See *infra* Figure 1 (depicting global M&A trends). This calculation is based on data from Thomson Reuters’ Investment Banking Deal Activity. *SDC Platinum Database*, THOMSON REUTERS, <http://financial.thomsonreuters.com/en/products/data-analytics/market-data/sdc-platinum-financial-securities.html> (last visited Apr. 2, 2017).

7. *Recap Database*, THOMSON REUTERS, <http://recap.com/> (last visited Apr. 2, 2017).

8. The source of Figure 1’s data is the Authors’ calculations based on the Thomson Reuters “SDC Platinum” database. *SDC Platinum Database*, *supra* note 6.

regulatory and marketing capacities. Thus, one explanation for the acquisition trend is that long-term investments in marketing and distribution trigger purchases for new discoveries. When large pharmaceutical firms cannot fill their marketing channels, they acquire companies to maintain a steady supply.

This interpretation of the acquisition spree, therefore, suggests that acquisitions constitute efforts to compensate for the lack of discovery by leading pharmaceutical companies. To utilize sunk investments in marketing and distribution, large pharmaceutical companies must acquire other companies with profitable discoveries when these acquirers are not producing valuable discoveries themselves. This is the conclusion reached by William Haseltine, who laments that the merger trend “reflects the failure of each company to discover and develop its own replacement pipeline.”⁹

A related lament is that because pharmaceutical firms enter into M&A transactions because they fail to develop new compounds, they also merge to hide larger shortcomings. Danzon et al. (2007) observe not only that mergers are a response to financial trouble, but that they are not a solution, either.¹⁰ They observe that financial hardship and patent expirations largely drive mergers, yet merged firms (after controlling for these troubles) experience slower profit growth than nonmerged firms.¹¹ Other anecdotal evidence confirms that the absorption costs of mergers are substantial enough to counteract many of the potential benefits of mergers.¹² These findings suggest that mergers might result from executive agency costs rather than from efforts to increase shareholder value.

Thus, the conventional wisdom interprets the current merger spree as a reflection of a faltering industry. Firms that initiate mergers do so because they suffer from weak returns and exhibit inadequate innovation, and these mergers are then burdened by high integration costs and low profitability. In this view, public policy, perhaps through merger review, should then intervene to discourage mergers of large pharmaceutical companies. If, after all, mergers are products of agency costs and reduced firm value, then any proffered efficiencies defense that justifies additional

9. William Haseltine, *Why Big Pharma Mergers Magnify Failures*, ATLANTIC (Mar. 11, 2009), <http://www.theatlantic.com/technology/archive/2009/03/why-big-pharma-mergers-magnify-failures/16892/>.

10. Patricia M. Danzon et al., *Mergers and Acquisitions in the Pharmaceutical and Biotech Industries* 4–5 (Nat’l Bureau of Econ. Research, Working Paper No. 10536, 2004).

11. *Id.* at 29–33.

12. A.T. KEARNEY, *MERGERS AND ACQUISITIONS IN THE HEALTHCARE INDUSTRY* (Aug. 2010), https://www.atkearney.com/documents/10192/256759/MA_in_Healthcare.pdf/6f7857c3-80d5-4020-89fc-8ef86abb94bc.

market concentration should be rejected. And, if mergers are evidence of shortcomings in pharmaceutical innovation, then perhaps policymakers should address this more foundational concern.

But this conventional wisdom rests on two flawed assumptions. First, it assumes implicitly or explicitly that the established firms *should* be the source of most major innovations; second, it assumes a static perspective on an industry that is undergoing significant structural change. The drug-development universe is a collection of heterogeneous firms and researchers, far more than what a few sets of large corporate labs could cover. The industry has always relied on R&D and on firm heterogeneity to innovate, and a diversity of research strategies and skills is only increasing as biological and other drug forms assume growing significance to medical care. Innovative outcomes are more likely to cover a wider space of activity and output if the industry structure includes a wide variety of players in multiple geographic locations. Consequently, rather than deliberating over how many established drug firms are necessary to generate optimal innovation, it might be more useful to understand the processes that maintain and generate industry heterogeneity.

Thus, even if the industry's largest firms are merging out of weaknesses, and even if these mergers fail to correct those weaknesses, these firms' failings do not mean that the industry as a whole is faltering. Those fearing both the causes and consequences of concentration look to large pharmaceutical firms to be the industry's profit leaders, primary sources of innovation, and principal avenues for marketing. But reports from industry leaders and reviews of medical research suggest that the industry is moving away from traditional sources of innovation; that physicians writing prescriptions are relying on new sources of information; and that large pharmaceutical firms are carving out a narrower space in the market for drug development, leaving important innovative space for entrants and specialists.

These changes color any evaluation of recent megamergers and suggest that their consequences—and the consequences of other changes in the industry's landscape—are far less certain. What is certain, however, is that the surge in acquisitions reflects a market that is both in transition and ripe for further study. Among the most pressing questions are whether these mergers permitted the accumulation of market power that led to higher prices, and whether these mergers reduced innovation activity.

II. PHARMACEUTICAL ACQUISITIONS, PRICE EFFECTS, AND PRICING STRATEGIES

Pharmaceutical prices in the United States have unquestionably increased substantially in the past two to five years.¹³ How much the increases stem from M&A, though, is a question with a more ambiguous answer. Well-publicized examples in which firms such as Turing, Horizon, and Valeant purchased companies with older products and then raised the prices of their products, often by many multiples, are highly visible.¹⁴ These companies also drew criticism from imposing high prices for specialized drugs, such as Gilead's Hepatitis C treatments and Mylan's EpiPen for allergic reactions.¹⁵ Yet established drug companies such as Pfizer and others have also steadily increased list prices during the past few years.¹⁶ It is beyond dispute that rising pharmaceutical prices pose fiscal dangers to both private and public budgets.¹⁷ It is not clear, however, whether the rising pharmaceutical prices stemmed from increased concentration in the industry.

Figure 2 estimates industry concentration based on the Hirschman Herfindahl Index ("HHI") for both the global and United States pharmaceutical markets.¹⁸ It appears that overall concentration in the

13. *Visualizing Health Policy: Recent Trends in Prescription Drug Costs*, KAISER FAM. FOUND. (Apr. 5, 2016), <http://kff.org/infographic/visualizing-health-policy-recent-trends-in-prescription-drug-costs/>.

14. See *Valeant & Shkreli-led Turing*, *supra* note 2 (discussing both Valeant & Turing's purchase of older drugs and raising the prices); see Rockoff & Silverman, *supra* note 2 (describing Valeant's purchase of life-saving heart drugs, and increasing the prices by 525 percent and 212 percent).

15. See Kozarich, *supra* note 2 (noting EpiPen's price increase from \$100 in 2009 to \$608 in 2017); Langreth, *supra* note 2 (noting Gilead's price increase to \$1,000 per pill for a twelve-week treatment for Hepatitis C).

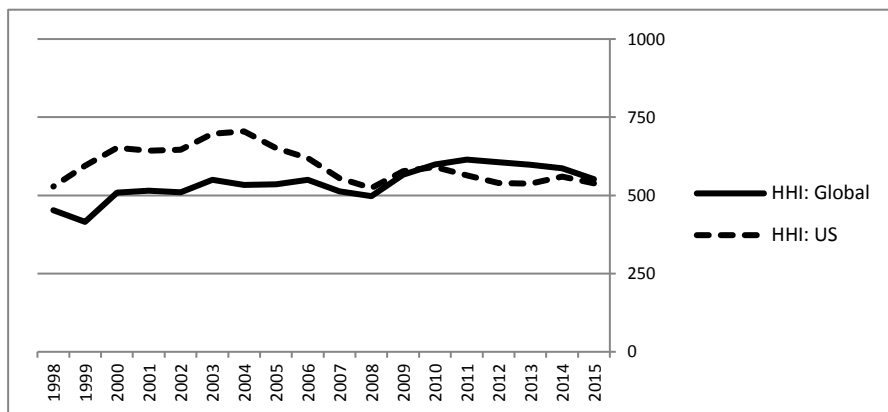
16. Ed Silverman, *Pfizer Just Raised Drug Prices by an Average of Nearly 9 Percent*, STAT NEWS (June 9, 2016), <https://www.statnews.com/pharmalot/2016/06/09/pfizer-drug-prices-turing-valeant/>.

17. Bradford R. Hirsch et al., *The Impact of Specialty Pharmaceuticals as Drivers of Health Care Costs*, 33 HEALTH AFF. 1714, 1718 (2014); Ifrad Islam, *Rising Cost of Drugs: Where Do We Go from Here?*, HEALTH AFF. BLOG (Aug. 31, 2015), <http://healthaffairs.org/blog/2015/08/31/rising-cost-of-drugs-where-do-we-go-from-here> ("The increase in drug costs—projected by the Centers for Medicare and Medicaid Services Office of the Actuary to be 12.6 percent in 2014—has far outpaced inflation, which has hovered between zero and 2 percent over the last three years; it has also outstripped growth in other medical costs. Pricewaterhouse Coopers (PwC), in its 2013 annual medical cost trend report, projected overall cost growth to be 6.5 percent in 2014 in the large employer market. In stark contrast, a recent Express Scripts analysis declared a 13.1 percent increase in prescription drug spend in the same period.").

18. See *infra* Figure 2 (depicting the concentration in the pharmaceutical industry). The Hirschman Herfindahl Index ("HHI") is a commonly accepted measure of concentration designed to reflect the pricing power that market actors have. It is calculated by summing the squares of the

industry is both low and relatively stable; the 500–700 range is well below the Department of Justice’s guidelines that consider HHI between 1,500 and 2,500 points to be moderately concentrated.¹⁹ Figure 2 demonstrates that recent price increases do not appear to correlate with market power based on greater overall concentration in the industry.

FIGURE 2: Pharmaceutical Industry Concentration, Measured by HHI, 1998–2015.²⁰



Additionally, increases in list prices for drugs can be somewhat misleading because they represent actual market prices. Insurance companies, hospital systems, pharmaceutical benefit managers (“PBMs”), and other payors with market power commonly negotiate deep discounts from list prices through a system of rebates and chargebacks. The health care industry has seen high levels of provider and payor consolidation in the last two decades due to inadequate antitrust enforcement. This consolidation raised health care prices for consumers while simultaneously enhancing market power of providers and payors when demanding discounts from pharmaceutical manufacturers.²¹ While

percentage market shares held by each firm in the market. For example, an industry consisting of two firms with market shares of 70 percent and 30 percent has an HHI of $70^2 + 30^2$, or 5,800. An industry with five firms, each with a 20 percent market share, is $20^2 + 20^2 + 20^2 + 20^2 + 20^2$, or 2,000. It ranges from near-zero (for a perfectly competitive marketplace with many firms, each with very negligible market shares), to 10,000 for a monopoly.

19. *Herfindahl-Hirschman Index*, U.S. DEP’T OF JUST.: ANTITRUST DIVISION, <https://www.justice.gov/atr/herfindahl-hirschman-index> (last visited Apr. 18, 2017).

20. The source of Figure 2’s data is from the Authors’ calculations, based on sales data from company annual reports (HHI is the sum of squared market shares).

21. BARAK D. RICHMAN, CONCENTRATION IN HEALTH CARE MARKETS: CHRONIC PROBLEMS AND BETTER SOLUTIONS 13 (JUNE 2012),

these negotiations are typically confidential and nontransparent, there are suggestions that discounts can reach as high as 40–50 percent off the listed prices.²² Other customers, such as the United States Department of Veterans Affairs (“VA”) and Medicaid in the United States, also typically receive prices at a discount from list prices (the VA through direct negotiation and Medicaid through statutory rebates).²³ Even with such discounts, overall drug spending is increasing in the United States and in many other countries.²⁴

Instead of prices correlating systematically with industry concentration, it seems that individual price increases are products of specific market structures and opportunities. Specifically, recent price increases appear to have emerged from changes in firm strategies rather than arising from an increase in overall market power. Some instances of price increases are consequences of firms exploiting opportunities to raise prices on generic drugs with few competing products. More generally, many established proprietary drug companies are placing greater emphasis on specialty drugs, including drugs based on traditional small cell science and those stemming from the biological science revolution, that have few competitors in their targeted market segments.²⁵ While these strategies reflect the presence of market power (i.e., there are few competing products in the biofunctional space where these price increases take place), they appear uncorrelated with changes in industry-wide concentration arising from M&A trends. Instead, they reflect changes in market segmentation strategy, in which firms target medical needs where there are few competing products.

This suggests that market power is better measured not in industry-wide measures, but instead along functional equivalents, which is how antitrust regulators typically scrutinize proposed acquisitions. More

http://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=5378&context=faculty_scholarship.

22. Carolyn Y. Johnson, *Secret Rebates, Coupons and Exclusions: How the Battle over High Drug Prices Is Really Being Fought*, WASH. POST (May 12, 2016), <https://www.washingtonpost.com/news/wnk/wp/2016/05/12/the-drug-price-arms-race-that-leaves-patients-caught-in-the-middle/>.

23. David Blumenthal & David Squires, *Drug Price Control: How Some Government Programs Do It*, COMMONWEALTH FUND (May 10, 2016), <http://www.commonwealthfund.org/publications/blog/2016/may/drug-price-control-how-some-government-programs-do-it>.

24. Tor Constantino, *IMS Health Study: U.S. Drug Spending Growth Reaches 8.5 Percent in 2015*, QUINTILESIMS (Apr. 14, 2016), <https://www.imshealth.com/en/about-us/news/ims-health-study-us-drug-spending-growth-reaches-8.5-percent-in-2015>.

25. Gregory Judd & Randy Vogenberg, *Planning a Specialty Drug Strategy Through 2020*, SOC’Y FOR HUM. RESOURCE MGMT. (May 4, 2015), <https://www.shrm.org/resourcesandtools/hr-topics/benefits/pages/specialty-drug-strategy.aspx>.

important, it suggests that pricing strategies will continue along a segmentation strategy, in which firms will seek market rigidity or a market niche in which there is a lag in opportunities for competitors to respond with competing products.

Such lags are highly sensitive to the surrounding regulatory framework that facilitates or deters entry. The primary source of such lags in the United States is the pharmaceutical regulatory system under the United States Food and Drug Administration (“FDA”). This time, lag means that companies with few, or no, competitors that raise prices on generic drugs will have the market to themselves until another firm is able to bring a competing drug through the Abbreviated New Drug Approval (“ANDA”) process, which often takes several years.²⁶ Similarly, a company that introduces a breakthrough drug at high prices will have the market to themselves until competitors are able to discover, develop, and bring competing drugs through the New Drug Approval (“NDA”) or Biological Licensing Approval (“BLA”) process; this, again, can take several years.²⁷

Reciprocally, market structures also allow for competitive reactions that limit pricing power. In many instances, new drugs that reach the market do lower list prices, deepen discounts, and reduce consumer prices. For instance, the introduction of AbbVie’s Viekira Pak into the Hepatitis C market in 2016 led to extensive price competition with Gilead based on discounts in the tens of thousands of dollars to pharmaceutical insurance and benefit management companies.²⁸ Similarly, Mylan steadily increased the list price of its patent-protected EpiPen. When Mylan acquired the product in 2007, the list price was a little over \$100, but its current price is over \$600, largely reflecting strong market preference for the company’s proprietary technology for injecting the allergic reaction drug.²⁹ Mylan indicated that it will also be launching a

26. Clay P. Wiske et al., *Options to Promote Competitive Generics Markets in the United States*, 314 J. AM. MED. ASS’N 2129, 2129 (Nov. 24, 2015).

27. For example, Gilead’s breakthrough drugs—Sovaldi (introduced in 2013) and Harvoni (introduced in 2014) for the treatment of Hepatitis C—had list prices in the United States (before discounts) approaching \$100,000 per treatment regimen. See Paul Demko, *New Hepatitis C Drug Costs Nearly \$100,000*, MOD. HEALTHCARE (Oct. 11, 2014), <http://www.modernhealthcare.com/article/20141011/MAGAZINE/310119928>.

28. Max Nisen, *Prices for the Miracle Drugs That Cure Hepatitis C Are Collapsing*, QUARTZ (Feb. 5, 2015), <http://qz.com/338840/prices-for-the-miracle-drugs-that-cure-hepatitis-c-are-collapsing/>.

29. Max Jacobs, *Don’t Blame Mylan for High Drug Prices*, FORBES (Nov. 7, 2016, 2:27 PM), <https://www.forbes.com/sites/realspin/2016/11/07/dont-blame-mylan-for-high-drug-prices/#5927e2a3ed5b>; Mannching Sherry Ku, *Recent Trends in Specialty Pharma Business Model*, 23 J. FOOD & DRUG ANALYSIS 595, 597 (2015).

generic version at about half the price, in anticipation of Teva Pharmaceuticals launching a generic competitor, while continuing to offer the branded product.³⁰ Again, while this is a market power issue, the pricing questions have little to do with industry-wide M&A trends. Indeed, industry reports in early 2017 suggest that alternatives to the EpiPen were rapidly eroding Mylan's market share.³¹

To the degree that market segmentation strategies are primarily responsible for price increases, it means that antitrust authorities should scrutinize specific biofunctional markets and evaluate mergers on whether a consolidated entity will have new pricing power within a specific pharmacological space or deter the entry of a pharmaceutical competitor. If AbbVie, for instance, were to seek to purchase Gilead, there could be a case for evaluating the deal because it would eliminate all competition within a specific biofunctional market. Similarly, Teva's recent acquisition of Allergan's generic drug lines warranted examination for potential market power in some product classes.³² But despite specific mergers that aggregate market power within a discernable submarket, it is not clear that the general trend in M&A activity warrants suspicion in terms of its impact on prices. The larger lesson is that maintaining a competitive pharmaceutical marketplace requires assessing and improving the surrounding regulatory structure, more so than deterring megamergers.

III. M&A AND R&D—A CHANGING MARKET FOR DISCOVERY

Perhaps even more important than the potential impact on prices, some observers and theorists suggest that M&A activity in the pharmaceutical sector might reduce innovative activity in the industry.³³ Commentators

30. Linda A. Johnson & Tom Murphy, *Drugmaker Mylan Launching Cheaper EpiPen Following Price-Hike Backlash*, TORONTO STAR (Aug. 29, 2016), <https://www.thestar.com/business/2016/08/29/drugmaker-mylan-launching-cheaper-epipen-following-price-hike-backlash.html>.

31. Arlene Weintraub, *EpiPen: Alternatives Snatch up Market Share as Mylan's Allergy Shot Falters: Report*, FIERCEPHARMA (Mar. 7, 2017, 9:01 AM), <http://www.fiercepharma.com/pharma/epipen-alternatives-snatch-up-market-share-as-mylan-s-allergy-shot-falters-report>.

32. The Federal Trade Commission ("FTC") evaluated the merger and ordered Teva to divest seventy-nine pharmaceutical products to preserve competition. See Press Release, Fed. Trade Comm'n, *FTC Requires Teva to Divest Over 75 Generic Drugs to Settle Competition Concerns Related to its Acquisition of Allergan's Generic Business* (July 27, 2016), <https://www.ftc.gov/news-events/press-releases/2016/07/ftc-requires-teva-divest-over-75-generic-drugs-rival-firms-settle>.

33. See BRUNO CASSIMAN & MASSIMO G. COLOMBO, *MERGERS AND ACQUISITIONS: THE INNOVATION IMPACT* 75 (2006).

not only worry that industry consolidation increases prices, but also that it reduces incentives to innovate.³⁴ These commentators express concern that large pharmaceutical firms exhibited diminishing R&D productivity—producing fewer discoveries, generating less valuable discoveries, and creating discoveries that represent more incremental and duplicative innovations.³⁵ In parallel, commentators suggest that the recent merger trend contributed to big pharma’s diminishing innovation, in part because mergers are often followed by layoffs in R&D personnel, changes in management and research priorities, and reductions in total R&D spending.³⁶

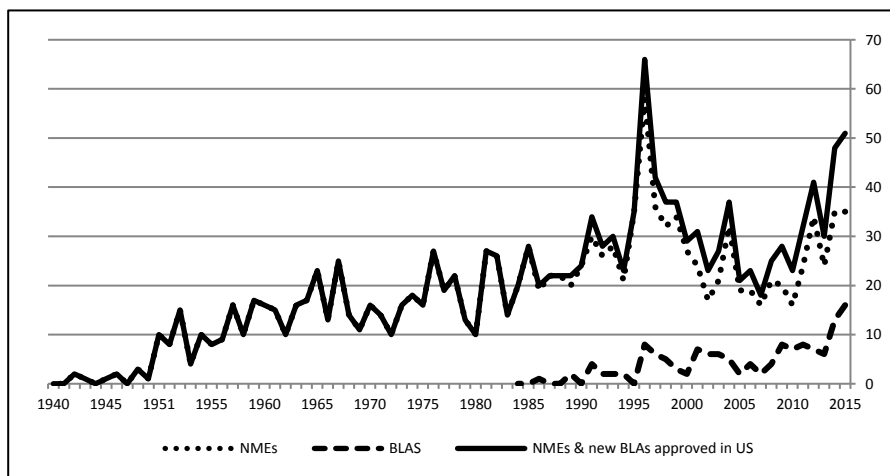
Our review of data measuring pharmaceutical innovation, however, tells a different story. First, even as merger activity in the United States increased over the past ten years, there has been a steady upward trend of FDA approvals of new molecular entities (“NMEs”) and new biological products (“BLAs”).³⁷ Hence, the industry has been highly successful in bringing new products to the market.

34. Giovanni Valentini, *Measuring the Effect of M&A on Patenting Quantity and Quality*, 33 STRATEGIC MGMT. J. 336, 338 (2012).

35. See, e.g., Fabio Pammolli et al., *The Productivity Crisis in Pharmaceutical R&D*, 10 NATURE REV. DRUG DISCOVERY 428, 428 (June 2011).

36. See, e.g., Justus Haucap & Joel Stiebale, *Research: Innovation Suffers When Drug Companies Merge*, HARV. BUS. REV. (Aug. 3, 2016), <https://hbr.org/2016/08/research-innovation-suffers-when-drug-companies-merge> (noting that research and development (“R&D”) and “patenting within the merged entity decline substantially after a merger”); see Peter Loftus et al., *In Drug Mergers, There’s One Sure Bet: The Layoffs*, WALL ST. J. (Apr. 29, 2014, 7:12 PM), <https://www.wsj.com/articles/SB10001424052702304393704579532141039817448> (noting how many workers have had to seek jobs elsewhere after large pharma mergers).

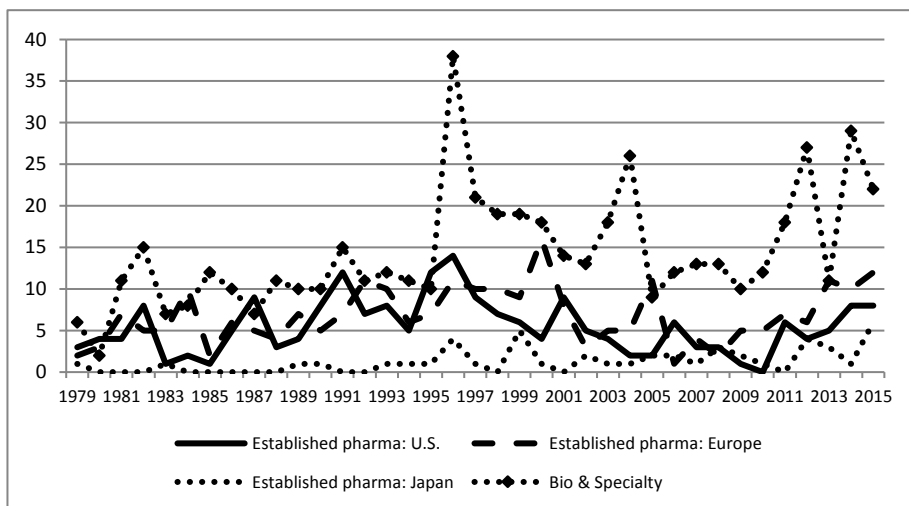
37. See *infra* Figure 3 (showing approvals from 1940 to 2015).

FIGURE 3: Trends in FDA Drug Approvals, 1940–2015³⁸

In addition, the diversity of firms carrying out R&D in the industry grew strikingly. Figure 4 denotes the status of firms receiving approvals from the FDA since 1979, and it illustrates the growing importance of “bio and specialty firms” and of (to a lesser degree) Japanese companies as drug developers for the United States and other markets. Although established United States and European firms continue to be important sources of new products, a vast array of specialized firms, ranging from large biological companies such as Amgen and Biogen to a globally distributed set of smaller specialists, now lead the industry. This fragmentation of the development base reflects both the increasing complexity of science underlying pharmaceutical products and the growing global scope of R&D expertise.

38. The peak in 1996–98 occurred following the implementation of the Prescription Drug User Fee Act (“PDUFA”), which allowed the United States Food and Drug Administration (“FDA”) to collect fees from drug manufacturers to fund the new drug approval process and thereby expedite approvals the cleared out a backlog of applications. The source of the Figure 4’s data is based on the Authors’ calculations using data from *Drugs@FDA: FDA Approved Drug Products*, U.S. FOOD & DRUG ADMIN., <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.ReportsMenu> (last visited Apr. 2, 2017) [hereinafter *Drugs@FDA*].

FIGURE 4: Status of Firms Receiving FDA Drug Approvals (NDAs & BLAs), 1979–2015³⁹



This fragmentation and diversification of discovery reveals one significant reason why pharmaceutical M&A activity increased. While established pharma companies such as Pfizer, Merck, GlaxoSmithKline (“GSK”), Eli Lilly, and Novartis continue to develop new drugs in their own labs, they are becoming increasingly dependent on acquiring other firms to fuel their new product lines. The locus of innovation is shifting from inside large firms to smaller start-ups and to firms operating in nontraditional geographic markets and complementary product markets. As a result, the pharmaceutical industry appears to be in significant structural transition, and the surge of acquisitions reflects that transition.

A number of forces are contributing to these industry changes. First, some medical researchers suggest that the frontier of discovery is moving away from small molecules—which has been the core of large pharma research—and toward biologics and delivery systems. One reason for this shift might be diminishing opportunities to discover new molecular innovations. Some academic physicians believe that the molecular space available for new discovery for small molecules is finite, and that current pharmacological technology is pressing against those upper limits.⁴⁰ Meanwhile, the growth of research on biologics is rapidly expanding, and

39. The source of Figure 5’s data is based on the Authors’ calculations based on data from the FDA’s report. *Id.*

40. For a discussion of technical challenges of the small-molecular drug discovery process, see Swen Hoelder et al., *Discovery of Small Molecule Cancer Drugs: Successes, Challenges and Opportunities*, 6 MOLECULAR ONCOLOGY 155, 169 (2012).

meaningful innovation is coming from research in biological interventions (some call this the “biological revolution,” as biologicals constituted more than one third of approvals in 2015). Traditional large pharmaceutical firms do not have dominant expertise in this scientific area, and the shift away from small-compound interventions and toward alternatives means a corresponding shift of innovation away from established pharmaceutical firms. Thus, established firms must pursue strategic acquisitions to sustain sales and pursue market opportunities now available from biological discoveries. The growth of new sources of discovery creates both growing scientific breadth in the industry’s underlying knowledge base and increasing market complexity, both domestically and globally.⁴¹

Another significant change in the market for innovation is the decline in costs and resources required to pursue meaningful innovation. The growing codification of scientific knowledge has increased the role of information technology (“IT”) on research. Thus, information for basic research is much easier both to transmit and to obtain. As a result, start-up biotech firms have been able to pursue meaningful innovations while remaining small. Consequently, competition for discovery of new pharmaceutical therapies is robust, and consolidation of big pharma companies does not seem to threaten the competitiveness of this upstream market for innovation.

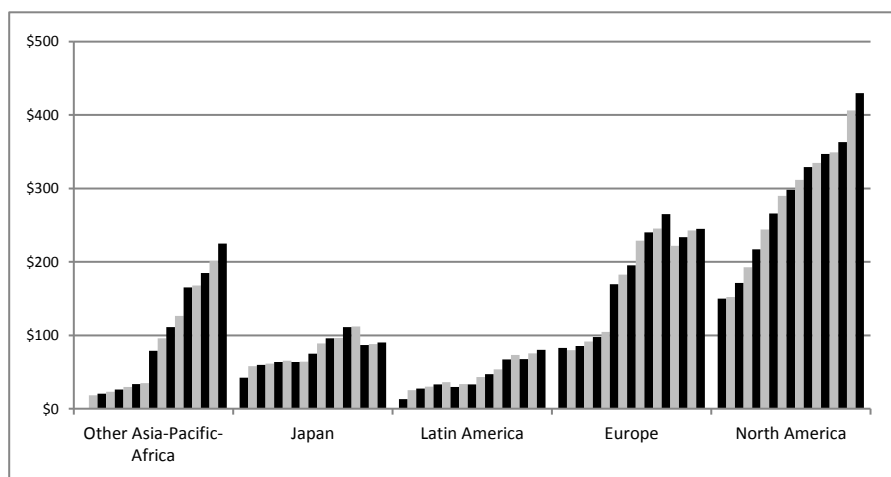
Yet while large and established pharmaceutical companies no longer have the dominant presence in discovery they once did, they still maintain an important comparative advantage over smaller firms from their ownership of large-scale marketing networks in multiple countries. Small firms developing drugs typically do not have the marketing capabilities required to bring those new drugs to global and segmented markets on their own. This need for global reach has been accelerated by the growth of pharmaceutical sales in emerging markets. Where the major markets were once concentrated in North America, Western Europe, and Japan, multiple emerging markets in Asia, South America, and elsewhere are now key targets for global pharmaceutical firms.⁴²

41. Abhirup Chakrabarti & Will Mitchell, *A Corporate Level Perspective on Acquisitions and Integration*, in 4 ADVANCES IN MERGERS AND ACQUISITIONS 1, 4–6 (Sydney Finkelstein & Cary Cooper eds., 2004); Elena Vidal & Will Mitchell, *Adding by Subtracting: The Relationship Between Performance Feedback and Resource Reconfiguration Through Divestitures*, 26 ORG. SCI. 1101, 1101 (2015).

42. QUINTILESIMS, TOP-LINE MARKET DATA: GLOBAL PHARMACEUTICAL MARKET SIZE & GROWTH BY REGION, 2014–2019, <http://www.imshealth.com/files/web/Corporate/News/Top-Line%20Market%20Data/Global%20Prescription%20Sales%20Information5%20World%20figures%20by%20Region%202015-2019.pdf> (last visited May 16, 2017) [hereinafter *Top-Line Market*

Indeed, China alone is now one of the top three pharmaceutical markets in the world, about level with Japan and markedly behind only the United States.⁴³ To succeed, established pharmaceutical companies now require global reach, while smaller players seeking to expand often need to acquire regional development and/or commercialization targets. Figure 5 highlights the growing importance of a broader range of pharmaceutical markets, particularly in the Asia-Pacific region, and Figure 6 depicts the proportion of acquisition targets that were based in the United States, Western Europe, and Asia between 1991 and 2015. The share of targets in the United States and Europe declined from over 40 percent each in the early 1990s to about 20–25 percent by 2015, while the share of targets based in Asia (other than Japan) grew rapidly, approaching 40 percent in 2015.

FIGURE 5: Trends in Global Pharmaceutical Sales in Billions, 1999–2015⁴⁴

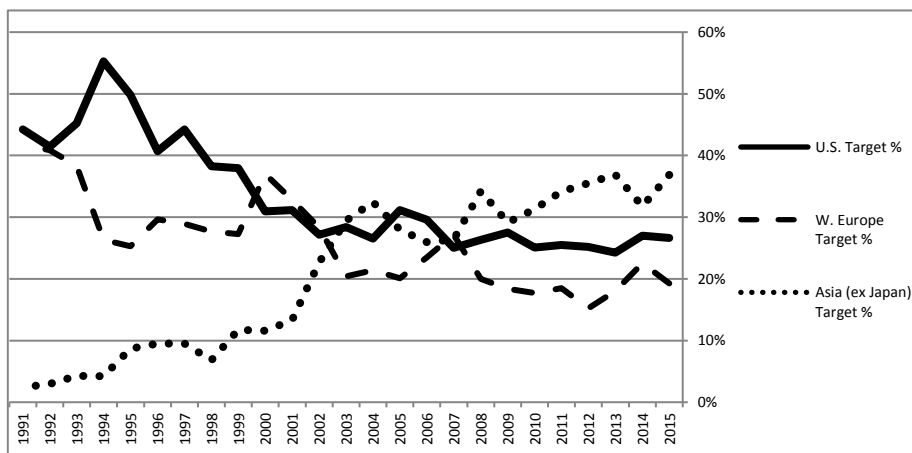


Data].

43. U.S. DEP'T OF COM.: INT'L TRADE ADMIN., 2016 TOP MARKETS SERIES: PHARMACEUTICALS COUNTRY CASE STUDY FOR CHINA 1 (2016), http://trade.gov/topmarkets/pdf/Pharmaceuticals_China.pdf.

44. The source of Figure 5's data was the Authors' calculations based on data from IMS Health. *Top-Line Market Data*, *supra* note 42.

FIGURE 6: Trends in Location of M&A Targets by Acquirers, 1991–2015⁴⁵



Serving such a disparate global market requires both refinements to products to suit local demand and local presence for development, regulatory, and marketing activity. While some of the expansion can build on existing internal skills or alliances with local partners, creating a strong local base in multiple markets commonly requires purchasing firms that already have a relevant presence.

For these reasons, many smaller firms with valuable discoveries opt to sell their innovative products, and often the entire company, to an established firm that wants to fill its pipeline.⁴⁶ Such deals provide an efficient way to leverage existing investments in marketing systems at the established companies, and they explain much of the growth in M&A activity that occurred during the past two decades.⁴⁷

45. *Description 2834: Pharmaceutical Preparations*, U.S. DEPT. LABOR, https://www.osha.gov/pls/imis/sic_manual.display?id=608&tab=description (last visited Apr. 18, 2017) (describing Standard Industry Classification (“SIC”) 2834 (Pharmaceutical Preparations)). The depicted deals total 83 percent of globally reported deals in 2015, with the remaining 17 percent distributed across the world. The source of Figure 6’s data was the Authors’ calculations based on Thomson Reuters’ Investment Banking Deal Activity. *SDC Platinum Database*, *supra* note 6.

46. LAURENCE CAPRON & WILL MITCHELL, *BUILD, BORROW, OR BUY: SOLVING THE GROWTH DILEMMA* 136 (2012).

47. Mid-sized and smaller firms in the sector—not just the traditional big-pharma firms—also commonly use acquisitions to gain access to capabilities that they need to develop further. In 2015, for instance, of 506 M&A deals listed in the Thomson Reuters Recap data base, 11 percent of the buyers were established pharmaceutical industry leaders, 23 percent were mid-sized pharma and life sciences firms, and 66 percent were smaller firms and diversifying entrants. Hence, M&A is as much or more part of the means by which newer actors attempt to build new positions in the sector. *Recap Database*, *supra* note 7.

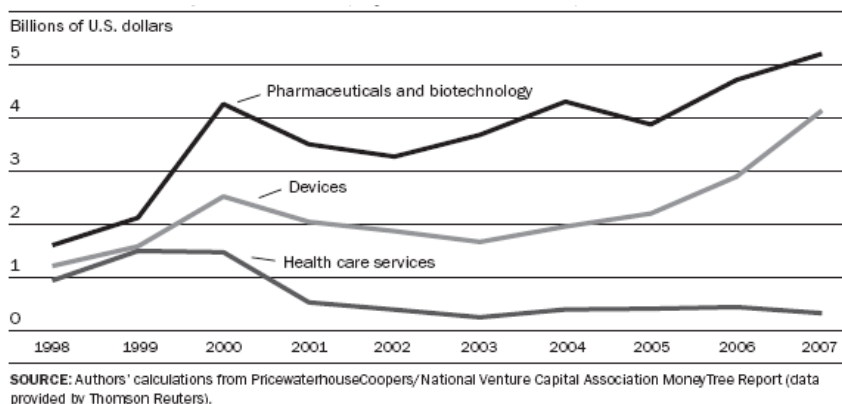
Another comparative advantage established firms have over start-ups is their access to the financing required to obtain FDA approval, and especially to fund Phase-III human trials or large scale trials at earlier phases. For this reason, start-ups frequently sell their discoveries to large pharmaceutical firms prior to FDA approval and commercialization. Accordingly, large pharmaceutical firms are occupying a different role in drug development. Rather than primarily being creators of innovation—investing in R&D and managing a soup-to-nuts operation—these firms are increasingly functioning as purchasers of innovations and are adding value to the downstream regulatory and commercialization processes.

Perhaps ironically, many of the megamergers contributed to, rather than squelched, the competitiveness of this process. Mergers often result in the departures of important executives, and many of those executives then form new ventures that aid in turning discoveries—often the discoveries they helped develop before departing to the large company—into commercialized products. One trend is to form small companies that purchase the rights to specific compounds, contract with firms to conduct the appropriate clinical trials to win FDA approval, and then sell to a large pharmaceutical company for distribution and marketing. Such ventures are called “virtual companies” because they conduct neither research nor clinical tests themselves, but manage the development-to-commercialization process through contracting agents. They signal a new disaggregation of the pharmaceutical industry that dilutes many concerns for industry concentration.

One remaining question is whether small companies—whether start-ups engaged in R&D, virtual companies that rely on contracting services, or even mid-sized clinical trial companies that take ownership of discoveries—will find the capital to pay for substantial clinical trials. Even if the industry is moving toward further disaggregation, megamergers might harm competition if it means fewer parties are available to finance the development process. But the emergence of venture capital (“VC”) in the health care sector helps mitigate any monopsony power that large pharmaceutical companies might have for new discoveries. Even though large pharmaceutical firms are increasingly relying on purchasing rather than producing innovation (it is likely that over 25 percent of total sales of the twenty largest pharmaceutical firms now come from in-licensed products), the flow of VC into the health sector has increased significantly in recent years, with health sector VC representing 31 percent of total VC investments in 2007.⁴⁸

48. See *infra* Figure 7 (noting the annual venture capital investment in the health care sector).

FIGURE 7: Annual VC Investment in the Health Care Sector, 1998–2007.



Although the number of VC investors declined during this recent economic downturn, VC will remain an important part of health care innovation in the years to come.

Whether VC is a reliable source of funding for Phase III and other human trials, however, is an open question. Venture capitalists view FDA review and Medicare and insurance reimbursement policies as sources of significant risk that steer VC investments toward firms that do not focus exclusively on health care. Though venture capitalists looked into funding Phase-III trials, they achieved few successes to date. The role of VC is especially important because although the market for discovery is vibrant, it is also fragile, with up to 50 percent of listed firms at risk of going bankrupt in 2017 and many currently trading at less than cash value.⁴⁹ If the finance and VC markets cannot adequately fund the innovation process, then large pharmaceutical firms with significant cash on hand and reliable sources of income from currently commercialized drugs will have an advantage in the market for purchasing discoveries.

Although VC and third-party funding slowed with the current downturn, companies of all sizes are still able to attract sufficient funding to carry discoveries forward, and the market should remain vibrant for players in addition to big pharma firms. This suggests that recent megamergers have not sufficiently concentrated either the market for discoveries to harm the rate of innovation. Thus, there remains an adequate number of parties capable of shepherding discoveries through

49. Michael Brush, *Dozens of Biotech Companies are 'Free' for Investors Taking*, MARKETWATCH (Feb. 16, 2016, 9:18 AM), <http://www.marketwatch.com/story/dozens-of-biotech-companies-are-free-for-investors-taking-2016-02-16>.

to commercialization.

In short, we are witnessing a major structural change in the locus of biomedical research. The three trends discussed herein—that innovation is increasingly occurring within start-ups, that large pharmaceutical companies are increasingly relying on in-licensed products, and that megamergers are potentially concentrating the market for buyers of innovation—will lead to major changes in drug discovery. Although it is unclear whether megamergers stifled innovation within this new industry paradigm, the data do not conclusively suggest that mergers have actually created harm.

IV. DOES M&A ACTIVITY DISRUPT RESEARCH AND PRODUCT INTRODUCTION?

Even if the surge in recent M&A activity has not reduced industry-wide drug approvals, some observers and theorists suggested that M&A deals might reduce innovative activity by disrupting innovative capabilities at the firm level. Because acquisitions require organizational changes at both the target and acquiring firms, many employees from both sides of a deal commonly seek alternative employment following an acquisition, either because they chose to move on or because of the downsizing that often occurs during acquisition integration. Integrating the different research, development, trials, and regulatory systems of the target and acquirer, meanwhile, is a complicated task. As a result, there is potential for disruption in R&D labs, clinical trials units, and other parts of the newly combined firm.

The question of whether acquisition deals systematically deter innovative activity is best answered from a longitudinal analysis of pharmaceutical firm performance. One of the authors in this Article recorded the number of deals by seventeen firms, including thirteen major established companies and four substantial pharma specialists, from 1985 to 2009. The seventeen firms undertook 556 M&A deals with reported value of \$67.6 billion during this period. For these same firms, we also gathered data from 1990 to 2014 for sales (\$6.0 trillion revenue in the twenty-five-year period), R&D expenditures (\$946 billion expenditure in the period), and drug approvals by the FDA (1,213 approvals), as well as the number of clinical trials initiated from 2000 to 2013 (14,614 trials). We then investigated whether firms with more acquisition deals had greater or lesser subsequent innovative activity. We caution that the investigation is exploratory; we cannot determine causality from the analysis, but can identify relevant longitudinal patterns.

We first consider the relationship between acquisitions and R&D expenditures. Panel A of Table 1 shows that firms with more M&A

activity in a five-year period, whether based on reported value or number of deals, tended to have lower R&D expenditures as a percentage of sales the next five years (i.e., the correlations were negative). In Panel B, we also examined selling, general, and administrative (“SG&A”) costs during the same period, which track closely with marketing expenditures, most commonly finding similar negative correlations. The core implication here is that firms that are most active in acquiring companies subsequently invested less in both internal R&D and marketing relative to their sales levels.

TABLE 1: Relationship Between Firms’ Levels of M&A Activity and Subsequent R&D and SG&A Expenditures as a Percent of Sales (Seventeen Firms)

| Correlations: M&A v. R&D & SG&A (Lagged Five-Year Periods) | Acquisition Value | Acquisition # |
|---|--------------------------|----------------------|
| Panel A. R&D/Sales Expenditure | | |
| Acquisitions, 1985–89 v. R&D/Sales, 1990–94 | -0.10 | -0.21 |
| Acquisitions, 1990–94 v. R&D/Sales, 1995–99 | -0.16 | -0.32 |
| Acquisitions, 1995–99 v. R&D/Sales, 2000–04 | -0.28 | -0.29 |
| Acquisitions, 2000–04 v. R&D/Sales, 2005–09 | -0.37 | -0.26 |
| Acquisitions, 2005–2009 v. R&D/Sales, 2010–13 | -0.05 | -0.06 |
| Panel B. SG&A/Sales Expenditure | | |
| Acquisitions, 1985–89 v. SG&A/Sales, 1990–94 | 0.20 | 0.25 |
| Acquisitions, 1990–94 v. SG&A/Sales, 1995–99 | -0.15 | -0.32 |
| Acquisitions, 1995–99 v. SG&A/Sales, 2000–04 | -0.17 | -0.24 |
| Acquisitions, 2000–04 v. SG&A/Sales, 2005–09 | -0.15 | -0.04 |
| Acquisitions, 2005–29 v. SG&A/Sales, 2010–13 | 0.01 | -0.06 |

Nonetheless, parsimony in R&D expenditure is not necessarily a negative sign for product development productivity. Instead, lower R&D and sales may reflect greater efficiency in R&D investments. The more important question is whether these acquisition-active firms also had lower success in bringing new products into clinical trials and, ultimately, to the market.

Table 2 reports the correlation relationships for three five-year periods of acquisition and subsequent clinical trial activity. The results in Panel A, for all clinical trials, suggest that greater M&A activity most commonly has, at least, a moderately positive relationship with bringing potential new drugs into human trials. The simplest interpretation is that acquisitions often help firms gain access to drugs for their clinical trials pipelines, complementing their internal development activities. Thus, even though internal R&D/sales ratios may decline, overall introduction into the clinical pipeline increases with greater M&A activity.

We then investigated whether the patterns differ by stage of clinical trial to explore whether the acquisitions tend to be targeted early in development pipelines (Phase I trials) or whether they take place closer to market entry (Phase III trials). Panel B, examining early-stage Phase I trials, offers mixed results, with negative relationships for two of three cohorts by acquisition value, but positive relationships for all cohorts by number of acquisitions. Panel C, examining later Phase III trials, has mainly positive correlations. There is some hint here, then, that firms undertaking larger acquisitions may be focused further down the pipeline (Phase III), while firms undertaking many smaller deals gain pipeline opportunities both early and late in the development phases (both Phase I and III). Overall, acquisitions appear to help firms gain access to potential products.

TABLE 2: Relationship Between Firms' Levels of M&A Activity and Launching Clinical Trials (Seventeen Firms)

| Correlations: M&A v. Clinical Trials and FDA Approvals (Lagged Five-Year Periods) | Acquisition Value | Acquisition # |
|--|--------------------------|----------------------|
| Panel A. All Clinical Trials | | |
| Acquisitions, 1995–99 v. Clinical Trials, 2000–04 | -0.13 | 0.41 |
| Acquisitions, 2000–04 v. Clinical Trials, 2005–09 | 0.09 | 0.30 |
| Acquisitions, 2005–09 v. Clinical Trials, 2010–13 | 0.52 | 0.47 |
| Panel B. Phase I Trials | | |
| Acquisitions, 1995–99 v. Phase I Trials, 2000–04 | -0.33 | 0.55 |
| Acquisitions, 2000–04 v. Phase I Trials, 2005–09 | -0.11 | 0.16 |
| Acquisitions, 2005–09 v. Phase I Trials, 2010–13 | 0.25 | 0.26 |
| Panel C. Phase III Trials | | |
| Acquisitions, 1995–99 v. Phase III Trials, 2000–04 | 0.18 | 0.01 |
| Acquisitions, 2000–04 v. Phase III Trials, 2005–09 | -0.04 | 0.23 |
| Acquisitions, 2005–09 v. Phase III Trials, 2010–13 | 0.57 | 0.39 |
| Panel D. FDA Approvals | | |
| Acquisitions, 1985–89 v. Approvals, 1990–94 | 0.39 | 0.36 |
| Acquisitions, 1990–94 v. Approvals, 1995–99 | 0.75 | 0.48 |
| Acquisitions, 1995–99 v. Approvals, 2000–04 | 0.09 | 0.49 |
| Acquisitions, 2000–04 v. Approvals, 2005–09 | -0.01 | 0.25 |
| Acquisitions, 2005–09 v. Approvals, 2010–13 | 0.51 | 0.42 |

Simply bringing a molecule into clinical trials, however, is no guarantee of market entry. Even at Phase III, products fail and never reach the market. Therefore, we examine the correlation between M&A activity and FDA approvals of new drugs, reported in Panel D. These correlations are almost all moderately positive. The most direct implication is that firms most active in M&A activity also are the firms most capable of bringing new drugs successfully into the market. The approvals may arise from drug pipelines that acquirers obtain with their targets. It is also possible, of course, that the opposite causality arises, in which firms that are most successful in introducing new drugs have resources needed to undertake more acquisitions. In either direction of causality, though, it appears that M&A activity is an active part of the strategy of the firms that are most successful in bringing new products to market.

These results are consistent with our observations in Part III of this Article: that acquisitions are often a consequence of, on one hand, the spread of the industry's innovation activity across a heterogeneous spectrum of firms and geographies, and on the other, a sustained comparative advantage by large traditional firms to bring products through the regulatory process and to market. These results further suggest that rather than disrupt innovative activity, M&A activity often supports product development and market introduction.

A deeper question is whether changes in firms' M&A activity—such as a temporal surge in acquisitions—might disrupt their innovation output. Table 3 measures the effect of whether a change in a firm's acquisition activity from one five-year period to the subsequent five-year period affects either the firm's clinical trials (reported in Panel A) or approvals (reported in Panel B). The question examined in Table 3 is whether firms that increase their rate of acquisitions, whether in value or number of deals, encounter disruptions as they engage in the extra effort of integrating their targets.

TABLE 3: Relationship Between Firms' Levels of M&A Activity and Changes in Clinical Trials and FDA Approval (Seventeen Firms)

| Change in M&A v. Change in Clinical Trials & FDA Approvals (Lagged Five-Year Increases) | Acquisition Value | Acquisition # |
|--|--------------------------|----------------------|
| Panel A. Change in Clinical Trials | | |
| Acquisition Change, 1995–99 to 2000–04 v. Trials Change, 2000–04 to 2005–09 | 0.13 | 0.01 |
| Acquisition Change, 2000–04 to 2005–09 v. Trials Change, 2005–09 to 2010–13 | -0.41 | -0.39 |
| Panel B. Change in FDA Approvals | | |
| Acquisition Change, 1985–89 to 1990–94 v. Approvals Change, 1990–94 to 1995–99 | 0.73 | 0.36 |
| Acquisition Change, 1990–94 to 1995–99 v. Approvals Change, 1995–99 to 2000–04 | -0.57 | -0.22 |
| Acquisition Change, 1995–99 to 2000–04 v. Approvals Change, 2000–04 to 2005–09 | 0.22 | 0.25 |
| Acquisition Change, 2000–04 to 2005–09 v. Approvals Change, 2005–09 to 2010–14 | -0.69 | -0.49 |

The evidence reported in Table 3 is mixed, showing that a change in acquisition activity has a volatile relationship with change in approvals and trials, sometimes positive and sometimes negative. The implication is that ramping up deal making can be helpful, but it also may disrupt existing routines and practices strongly enough to hamper pipeline activities.

Recent history offers several examples of both negative and positive changes arising from accelerated acquisition activity. Pfizer, for instance, grew its deal-making activity during the early 1990s, with several moderate-sized deals such as purchasing Schneider NAMIC U.S.A. Corp. and making equity investments in Neurogen and Incyte, gaining

technology that led to gains in trials and approvals in the late 1990s.⁵⁰ The company went through another burst of acquisition activity in the late 1990s and early 2000s, including deals for Warner-Lambert (gaining the anti-cholesterol drug Lipitor) and Pharmacia (gaining the anti-inflammatory drug Celebrex), which helped the company become the world's largest pharmaceutical company.⁵¹ But the new growth deals were followed by a decline in trials and approvals in subsequent years and Pfizer eventually lost its number one revenue position. Reliance on gaining products via deal making may have inhibited the ability to bring new products into the pipeline.

Sometimes, however, what appear to be disruptions can instead prepare the foundation for future growth. Abbott (now AbbVie) increased its deal making in the late 1990s, buying multiple companies and attempting to acquire Alza in 1999 (\$7.3 billion).⁵² Time spent on due diligence, integration, and break up appears to have detracted attention from the company's ongoing clinical activity and slowed subsequent trials and approvals. Yet this deal activity helped lay the groundwork for its later acquisition of BASF/Knoll in 2000 (for \$6.9 billion), which brought with it the technology that led to trials and approvals of Humira, which is used to treat rheumatoid arthritis and other autoimmune diseases, and that subsequently became the world's top selling drug later in the 2000s.⁵³ Similarly, Glaxo (now GSK) exhibited a burst of M&A activity in the late 1990s, particularly with the \$14.3 billion acquisition of Burroughs Wellcome in 1994–95.⁵⁴ The work required to assess and integrate the deals appeared to have disrupted subsequent pipeline activity in the early 2000s, but it also laid the groundwork for future growth, with GSK reaching the status as one of the world's most successful pharmaceutical companies during the 2000s.⁵⁵

Clearly, the negative relationships signal some concern about deal

50. J.A. ROELS, *THE ORIGIN AND THE EVOLUTION OF FIRMS: INFORMATION AS A DRIVING FORCE* 164 (2012).

51. Matthew Herper, *Pfizer Buys Pharmacia for \$60 Billion*, *FORBES* (July 15, 2002, 7:53 AM), <https://www.forbes.com/2002/07/15/0715pfe.html>.

52. James P. Miller, *Abbott Laboratories to Purchase Alza for Stock Worth \$7.3 Billion*, *WALL ST. J.* (June 22, 1999, 12:01 AM), <https://www.wsj.com/articles/SB930002503336706177>.

53. Thomas M. Burton, *Abbott Laboratories Agrees to Buy BASF's Knoll Pharmaceutical Unit*, *WALL ST. J.* (Dec. 15, 2000, 12:13 PM), <https://www.wsj.com/articles/SB976832374667325423>.

54. Richard W. Stevenson, *Glaxo Offers \$14 Billion for Wellcome*, *N.Y. TIMES* (Jan. 24, 1995), <http://www.nytimes.com/1995/01/24/business/company-news-glaxo-offers-14-billion-for-wellcome.html>.

55. Sylvia Pfeifer, *The Drugs Don't Work for GlaxoSmithKline*, *TELEGRAPH* (Sept. 9, 2007, 12:01 AM), <http://www.telegraph.co.uk/finance/migrationtemp/2815417/The-drugs-dont-work-for-GlaxoSmithKline.html>.

activity, but it is important not to overstate the concerns. Once firms settle at a new rate of deal activity, they are likely to learn how to handle the new level and return to more positive patterns. Nonetheless, the patterns do raise cautionary notes for pharmaceutical managers. They also offer warning signals for antitrust regulators that are being told of efficiencies purported to arise from a proposed merger.

V. UNTRADITIONAL SOURCES OF ANTICOMPETITIVE HARM: MARKETING AND REGULATORY BOTTLENECKS

The previous three Parts of this Article suggest that broad trends in pharmaceutical acquisitions, and recent megamergers in particular, do not present traditional competition concerns for pharmaceutical prices and output. Research and discovery remain robust, albeit commonly from small firms pursuing large molecules and biologics rather than the small molecule discoveries that built the current pharmaceutical giants. Reductions in the cost of doing research, actualized by merging two research departments into one, enable entry and facilitate active competition for new discoveries. Even if the internal research productivity of some large pharmaceutical companies has declined, these firms have also become purchasers of innovation. This is true even as these firms continue as creators of innovation, and their purchases fuel the discovery process and enable the commercialization of many new products. The rise of virtual companies, companies that contract to do Phase-III human trials, and other small facilitating companies (some staffed by executives who were dismissed by newly merged giants) built an active and competitive market for commercializing discoveries. And even if a surge in firm M&A activity sometimes dulls innovative productivity, acquisitions appear to be an important part of both sustaining product development and even laying the foundation for long-term innovation activity. These developments mitigated most concerns that megamergers would reduce the competitiveness of discovery.

This Part explores two additional sources of concern about the sector's growing merger activity: whether industry concentration in marketing and distributing pharmaceuticals will distort consumption (and thereby increase prices or disrupt innovation strategies), and whether industry concentration causes regulatory bottlenecks that result in anticompetitive consequences.

A. New Systems of Distribution

Pharmaceutical sales remain highly influenced by the effectiveness of targeted marketing, and large pharmaceutical companies have therefore invested heavily in specialized sales forces. Many companies treat these

investments as fixed costs that cannot vary with the firm's research productivity, so firms purchase discoveries to maximally utilize the sales force capacities. Treating sales forces as fixed costs that would go unutilized without actively marketed products is one leading explanation for the steady frequency of acquisitions and the surge of megamergers.

The importance of sales forces accordingly attracts competition concerns when two companies with significant marketing operations decide to merge. Concentration in the market for pharmaceutical sales and distribution might lead to market power and all of its ill effects, including squeezing out superior competing products, higher prices, foreclosing possible entry by innovative competitors, and diminished consumer choice. But two significant changes in the marketing of pharmaceuticals might alleviate these competition concerns, and these mergers instead might reflect large pharmaceutical companies' shared perception that the industry has great excess marketing capacity that is being displaced by alternative distribution mechanisms.

One recent development affecting, and perhaps blindsiding, pharmaceutical marketing is the growing popularity of health care IT, including the proliferation of medical protocols. Whereas pharmaceutical marketing relies on the assumption that physicians prescribe drugs based on personal familiarity and comfort with certain compounds, the growth of electronic medical protocols would lead physicians to instead rely on codified instructions disseminated through IT systems.

The promise of IT to transform the delivery of medicine is not a new idea—health policy analysts have long been enthusiastic about its potential to bring more consistency to medical services, reduce errors, and constrain costs. And even as entrenched barriers impede the spread of systematized IT medicine,⁵⁶ including the training of doctors, the use of IT and electronic standardized protocols is growing in several systems, such as Kaiser Permanente's HealthConnect program. Moreover, enthusiasm for, and recent investments in, cost-effectiveness research might also stimulate greater use of electronic protocols. If cost-effectiveness research can document the comparative usefulness of alternative regimens, then electronic protocols would swiftly spread the information and standardize treatments.

The growing importance of PBMs also marks a change in how drugs are prescribed and consumed. PBMs purchase drugs in bulk on behalf of insurers and use formularies and coverage tiering to direct insureds (and

56. Susan Denzter, *Health Information Technology: On the Fast Track at Last?*, 28 HEALTH AFF. 320, 320 (2009).

thus prescribing physicians) toward certain prescriptions. The rise of PBMs leaves less latitude to physicians and patients in selecting particular drugs for prescriptions and means that companies must now direct pharmaceutical marketing information at PBMs, rather than individual physicians. A similar development occurred in the early 1990s, when the Clinton Health Plan proposed greater monitoring and restrictions on the selection of prescriptions.⁵⁷ Large pharmaceutical companies recognized that prescription selections would reduce the value of large sales forces, and these firms transferred investments away from traditional marketing and toward purchases of PBMs. The attempts to use the PBMs to generate profitability failed dismally, however, and the three major pharmaceutical companies that acquired PBMs (SmithKlineBeecham, Eli Lilly, and Merck) subsequently divested or spun them off, typically at losses or with significantly lower market capitalization than their acquisition costs. In turn, though, the PBM sector is now a vibrant part of the pharmaceutical value chain, including standalone PBMs and PBMs that are units within health insurance companies and drug store chains. Thus, the failed acquisitions of the PBMs by pharmaceutical leaders did not lead to failure of industry structure. Instead, the failures led to successful changes in market structure.

The impact of cost-effectiveness research, the growing use of IT, and the consolidated drug selections and purchases by PBMs could potentially obviate the need for vast marketing teams and sales forces. The information required by treating physicians would be transmitted by electronic mechanisms rather than in-person instruction sessions with sales representatives, and many prescription decisions might be removed from individual physicians altogether and instead given to well-informed bulk purchasers. Large pharmaceutical companies might have already recognized that these seismic changes are afoot, and their pursuit of recent megamergers might reflect their need to address overcapacity in marketing and sales. This would mean that market concentration in this downstream market should not translate into anticompetitive consequences.

While it is still unknown how significantly information systems will impact physician treatments and the issuances of pharmaceutical prescriptions, the growth of electronic protocols is potentially another major development that could transform the competitive structure of the pharmaceutical industry. An accurate competitive analysis would have

57. Walter A. Zelman, *The Rationale Behind Clinton Health Care Reform Plan*, 13 HEALTH AFF. 9, 10 (1994).

to take these changes into account, and future research could fruitfully examine the effect of electronic protocols both on physician behavior and on the usefulness of pharmaceutical sales representatives.

B. The Remaining Bottleneck: FDA Approval

The one area that seems to have the potential for competitive harm through market concentration is the process of obtaining regulatory approval. We interviewed several industry experts deeply familiar with the regulatory process. Consistent with discussions in the health services literature,⁵⁸ the experts suggest that the regulatory process remains a nonstandardized, and even personalized, process. It consequently rewards certain competencies that are in short supply and difficult to replicate. As one expert on the regulatory process remarked:

I don't think you'll ever do away with the need of regulatory specialists who interface between your data and decision making. [This will become increasingly important as] we not only have approval but we have payment, which has been connected in Europe for a while, [and] it's going to be connected in the U.S. It has to be. And so you'll need people who can navigate that no matter what.⁵⁹

Others we interviewed expressed a similar concern, that the regulatory process remains a bottleneck, in part because of the complexity of the regulatory demands and the differences in regulatory requirements across jurisdictions. While many contract research organizations have expertise in the regulatory process at the FDA, each class of products requires specific regulatory insight and knowledge. Consequently, recent entrants to the value chain for drug commercialization are challenged to translate industry success into an effective interface with regulators. Although there appears to be entry into the markets for discovery and commercialization, it is less apparent that there is effective entry into this regulatory phase that requires nonmarket capabilities.

With the recent passage of the 21st Century Cures Act,⁶⁰ the FDA will soon institute some reforms on its drug approval process. Perhaps this regulatory reform will reduce the centrality of certain skills, relationships, and knowhow that facilitates the FDA and other government agency approvals. Perhaps it will make the regulatory approval process more accessible to developers, thereby increasing meaningful competition.

58. See generally Robert M. Califf, *Benefit-Risk Assessments at the US Food and Drug Administration: Finding the Balance*, 317 J. AM. MED. ASS'N 693, 693 (2017) (noting the FDA's "system of rigorous, independent premarket assessment" that it uses when making marketing decisions).

59. Interview with Barak Richman, Will Mitchell, Elena Vidal, and Kevin Schulman (Spring 2009).

60. Pub. L. No. 114-255, 130 Stat. 1033 (2016).

But the novel technologies envisioned by the 21st Century Cures Act will require the development of new predictable, scientific, and transparent approval pathways. The presence of a regulatory bottleneck does expose a vulnerability to market concentration. If few firms possess the ability to navigate through the regulatory process, then mergers among those firms could translate into harm to competition. Our interviews suggest that the regulatory process and the possibilities for regulatory reform deserve attention as the consequences of megamergers are evaluated and scrutinized.

Market access through the reimbursement process of public and private payors is an additional hurdle to product adoption and uptake in the market. Similar to the regulatory process, the reimbursement process requires specialized insights and knowledge that provide additional uncertainty in the economic model for drug development. This specialized knowledge and additional risk posed by this step could also inhibit investment in early stage life sciences companies.

CONCLUSION

The global pharmaceutical industry is exhibiting meaningful structural changes, evidenced most clearly by ongoing growth in industry-wide M&A deals. This exploratory review finds evidence that the predominant concerns over megamergers among pharmaceutical giants might be misplaced. Changes in the scientific landscape of competitive innovation generated a vibrant marketplace for discovery, which megamergers do not necessarily threaten and instead might actually invigorate. Although megamergers may create some monopsony power for the purchase of discoveries, an active VC and biotech financing market, along with speculating contract research organizations and virtual companies, would counteract that. And the development of alternative information mechanisms to spread pharmaceutical information and effectiveness data, which would inform physicians and bulk purchasers of drugs, reduces the importance of pharmacy sales representatives, thus mitigating any competition concerns with downstream drug marketing and distribution.

These are some of the structural changes transforming the pharmaceutical industry, so any evaluation of mergers and market concentration would need to consider a wide array of dynamic forces. Among the other significant developments on the industry's horizon include the potential for regulated pricing on small molecules, including reference pricing in reimbursement policies and direct negotiations in Medicare Part D; the rising potential of biosimilars (generic biological drugs) and competition among biologics, which began several years ago

in Europe and Canada following the European Medicines Evaluation Agency and Health Canada's approvals and is now beginning to occur in the United States; emerging export markets in Brazil, Russia, India, China, and South Africa ("BRICS") and a changing international marketing landscape; and the all-important possibility of health reform, particularly as it might change the market and demand for biologics.

Partially because of this rapidly changing industry, and also partially because of the exploratory nature of this inquiry, this review of industry mergers identified few strong conclusions. Nonetheless, it identifies several areas for important future research: (1) whether there is an efficient finance market for the commercialization of drugs, and whether mergers create monopsony power for discoveries, or whether other industry players can emerge to commercialize discoveries; similarly, whether health care VC matures to promote promising technologies, or whether reimbursement and regulatory risk continue to drive VC dollars away from the health care sector; (2) how IT and electronic protocols will affect physician behavior, how they might standardize treatments and reduce costs, and how cost-effectiveness research affects these protocols; additionally, whether the introduction of IT can affect physician behavior at all, or if the training of physicians needs to change to capitalize on the potential efficiencies from IT and electronic protocols; and (3) how the regulatory process is changing, precisely why there are some firms able to achieve regulatory approval whereas others cannot, and why regulatory interface remains a scarce competency, and how the regulatory process could be streamlined to reduce bottleneck effects and vulnerability to market concentration. These questions should guide future inquiries into how merger activity and other dynamic market changes will shape industry performance and whether those changes translate into a clear direction for innovation and competition policy.